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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,354	12/06/2001	C. Frank Bennett	RTS-0348	5827

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	7

DATE MAILED: 01/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/003,354	BENNETT ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-15,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-15,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

Applicant's Amendment B, filed 12/12/02 in Paper No. 6 is acknowledged. Claims 16-18 were canceled. Claim 15 was amended. Currently claims 1, 2, 4-15, 19 and 20 are pending in the instant application.

Applicant's arguments for enablement of claims 15-18 are moot in view of Applicants canceling claims 16-18 and amending claim 15 to read on a method of inhibiting the expression of phosphatidylinositol-4-phosphate 5-kinase, Iα *in vitro.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4-15, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Honda et al. (Cell, 1999 Vol. 99: 521-532) Loijens et al. (Journal of Biological Chemistry, 1996 Vol. 271:32937-32942), in further view of Weintraub (Scientific American, 1990 pages 40-46) Baracchini et al. [U.S. Patent No. 5801154] and Fritz et al. (Journal of Colloid and Interface Science, 1997 Vol. 195:272-288).

This rejection is maintained for the reasons of record for rejection of claims 1, 2, 4-15, 19 and 20, as set forth in the Office action, mailed 9/11/02, in Paper No. 5.

2. Applicant's traversal and request for reconsideration and withdrawal of the 35 U.S.C. 103, rejection against claims 1, 2, 4-14, 19 and 20 has been fully considered. Applicants argue that Honda et al. disclose only the biological role of phosphatidylinositol-4-phosphate 5-kinase, but do not teach or suggest the use of antisense compounds of any type to target and inhibit the expression of phosphatidylinositol-4-phosphate 5-kinase Iα. Applicants further argue that Loijens et al. disclose the peptide sequence of phosphatidylinositol-4-phosphate 5-kinase Iα and the tissue distribution of phosphatidylinositol-4-phosphate 5-kinase Iα, but does not teach or suggest the use of antisense compounds of any type to target and inhibit the expression of phosphatidylinositol-4-phosphate 5-kinase Iα. Applicants further argue that Weintraub only discusses the use of antisense as a research tool, but does not teach or suggest the use of antisense compounds of any type to target and inhibit the expression of phosphatidylinositol-4-phosphate 5-kinase Iα. Applicants further argue that Baracchini et al. and Fritz et al., in general terms, disclose modifications and carrier systems for antisense oligonucleotides, but do not teach or suggest the use of antisense compounds of any type to target and inhibit the expression of phosphatidylinositol-4-phosphate 5-kinase Iα.

Applicant's arguments have been fully considered, but are not found persuasive. The specification at page 90, lines 22-25 states, "A summary of the target sites of the variants is shown in Table 2 and includes GenBank accession number U78576.1 representing the variant PIP5Kα1, incorporated herein as SEQ ID NO:3".

Loijens et al. disclose a nucleotide sequence with accession number U78576 (see Figures 1 and 2). The disclosure of Loijens et al. is identical to SED ID NO:3 of the instant invention

(see Figure 1). Loijens et al. further disclose the deduced amino acid sequence of PIP5Kα1 from the PIP5Kα1 cDNA.

Milligan et al. (Journal of Medicinal Chemistry, 1993 Vol. 36:1923-1937) teach making an antisense oligonucleotide if the mRNA sequence (or cDNA) is known:

> Antisense oligodeoxynucleotides (ODNs) have been proposed as a major class of new pharmaceuticals. In general, antisense refers to the use of small, synthetic oligonucleotides, resembling single-stranded DNA, to inhibit gene expression [references omitted]. Gene expression is inhibited through hybridization to coding (sense) sequences in a specific messenger RNA (mRNA) target by Watson-Crick base pairing in which adenosine and thymidine or guanosine and cytidine interact through hydrogen bonding (Figure 1). These simple base-pairing rules govern the interaction between the antisense ODNs and the cellular RNA, allowing the design of ODNs to target any gene of a known sequence (see Milligan et al., at p. 1923).

As stated in the previous Office Action, one of ordinary skill in the art would have been motivated to make antisense nucleic acids targeting phosphatidylinositol-4-phosphate 5-kinase Iα since Honda et al. and Loijens et al. taught phosphatidylinositol-4-phosphate 5-kinase Iα involvement in membrane ruffle formation, regulated secretion and signal transduction. As stated in the previous Office Action, one of ordinary skill in the art would have been motivated to inhibit the expression of one phosphatidylinositol-4-phosphate 5-kinase Iα variant over another since Loijens et al. taught PIP5KIα2 and PIP5KIα3 as splice variants of PIP5KIα1 which permit comparative studies of each isoforms. As stated in the previous Office Action, it would have been obvious to make antisense oligonucleotides encoding phosphatidylinositol-4-phosphate 5-kinase Iα since Weintraub taught antisense nucleic acids can selectively inhibit the activity of genes and gene expression and antisense techniques are tools for probing the functions of individual genes. Provided with the teachings of Weintraub, one in the art would clearly have been motivated to use antisense in the comparative studies, suggested by Loijens et al., for

example. As stated in the previous Office Action, one of ordinary skill in the art would have been motivated and had a reasonable expectation of success in modifying antisense oligonucleotides since the prior art has taught the desirable benefits of such oligonucleotides are often preferred over native forms because of enhanced cellular uptake, enhanced affinity for nucleic acid target, increased stability in the presence of nucleases and the exhibition of high colloidal stability with low toxic side effects as required for biological experiments (Baracchini et al. and Fritz et al.), for example.

Further, one would have been motivated to use antisense as suggested by Weintraub in elucidating the role of PIP5K1α regulated secretion, cytoskeletal dynamics and signaling cascades as suggested by Loijens et al.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 recites, "differentially inhibits". "Differentially inhibits" is a relative term which renders the claim indefinite. The term "differentially inhibits" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of "differentially inhibits" and one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Conclusion

Claims 1, 2, 4-15, 19 and 20 remain rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned is (703) 746-8693.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196

tcg

January 23, 2003

SEAN McGARRY
PRIMARY EXAMINER
1635